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HINES, JANA A				
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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

# Office Action Summary

## Application No.

10/795,873

## Applicant(s)

HERMET ET AL.

## Examiner

JaNa Hines

## Art Unit

1645

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --  
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

## Status

- 1) ☒ Responsive to communication(s) filed on 25 November 2008.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

## Disposition of Claims

- 4) ☒ Claim(s) 1-27 and 29-38 is/are pending in the application.
- 4a) Of the above claim(s) 11, 12, 18-22 and 29-36 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-10, 13-17, 23-27, 37 and 38 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

## Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

## Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

## Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO/SB/08)  
Paper No(s)/Mail Date \_\_\_\_\_
- 4) ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date \_\_\_\_\_
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: \_\_\_\_\_

**DETAILED ACTION**

***Continued Examination Under 37 CFR 1.114***

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on November 25, 2008 has been entered.

***Amendment Entry***

2. The amendment filed November 25, 2008 has been entered. The examiner acknowledges the amendments to the specification. Claim 1 has been amended. Claims 11-12, 18-22 and 29-36 are withdrawn. Claim 28 is cancelled. Claims 1-10, 13-17, 23-27 and 37-38 are under consideration in this office action.

***Withdrawal of Rejections***

3. The following objections and rejection have been withdrawn in view of applicants' amendments and arguments:

a) The rejection of claims 1-5, 8, 10, 14-17, 23-28 and 37-38 under 35 U.S.C. 103(a) as being unpatentable over Doshi et al., in view of Zierdt et al;

b) The rejection of claims 6 and 7 under 35 U.S.C. 103(a) as being unpatentable Doshi et al., and Zierdt et al., further in view of Cathey et al; and

c) The rejection of claims 9 and 13 under 35 U.S.C. 103(a) as being unpatentable over Doshi et al., and Zierdt et al., further in view of Besson-Faure et al.

### ***Response to Arguments***

4. Applicant's arguments with respect to claims 1-10, 13-17, 23-27 and 37-38 have been considered but are moot in view of the new ground(s) of rejection.

### ***New Grounds of Rejection in view of Applicants Amendments***

#### ***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

5. Claims 1-5, 8, 10, 14-17, 23-28 and 37-38 are rejected under 35 U.S.C. 103(a) as being unpatentable over Doshi et al., (US Patent 5,766,552) and Aunet et al., (US Patent 4,933,092) in view of Zierdt et al., (J. of Clinical Microbio. 1982. Vol. 15(1):74-77).

The claims are drawn to a method for detecting contaminating microbes possibly present in a blood product comprising blood cells comprising: a) subjecting a sample of

the blood product to an aggregation treatment of the blood cells, b) substantially eliminating aggregates formed in step (a) by passage of the sample over a first filter allowing passage of contaminating microbes, but not cell aggregates, c) selectively lysing residual cells of the filtrate obtained in step (b), d) adding a marker agent to label the contaminating microbes either during step (a) or step (b), e) recovering the contaminating microbes by passage of the lysate from step (c) over a second filter with a pore size of about 0.3 $\mu$ m to less than 1 $\mu$ m which retains contaminating microbes and allows passage of cellular debris, and f) analyzing material on the second filter to detect labeled contaminating microbes possibly retained by the second filter, the method being performed in an enclosed and sterile device. The dependant claims are drawn to permeabilization agents, detergents, marker agents, blood products, antibodies, lectins, the filters and the device.

Doshi et al., teach that the separation of serum or plasma from whole blood is extremely important since it is difficult to conduct the analysis of dissolved blood components without interference from red blood cells (col. 1, lines 47-50). Red blood cells (RBC) are removed from whole blood samples by contacting a whole blood sample with an agglutinating agent (col. 7, lines 25-28). The agglutinating agents allow for the quick and efficient formation of clusters of RBC, be fast acting, have short reactivation time, are non-specific to blood types, and be stable and inexpensive (col. 5, lines 32-34). Doshi et al., teach antibodies as agglutinating agents since they are reactive and well known for agglutinating erythrocytes (col. 7-8, lines 66-6). These antibodies should recognize antigenic surface constituents such as glycoproteins (col. 8, lines 6-10). By

contacting the RBC with agglutinating agent, the cells are agglutinated and trapped by the pad while the remainder of the fluid sample flows through readily (col. 6, lines 10-15). Doshi et al., teach the efficiency of filtration, along with the lysis of RBC wherein whole blood is passed through the filter and plasma is retained (col. 8, lines 54-56). Doshi et al., teach the removal of the RBC clusters by filtration (col. 11, lines 40-41). The preferred filtration uses a porous absorbent pad with mesh or pore size being from about 20 to about 500 microns (col. 62-65). This is within the instantly claimed size of pores for the first filter. The secondary filter is used to trap red blood cells and has a very small pore size to permit plasma to pass (col. 12, lines 1-11). Doshi et al., teach having a reactant pad through which the fluid flows to allow for the production of a detectable signal (col. 14, lines 39-41). The analyte reacts with the reagents to produce a detectable signal such as dyes, particles, and proteins with visible extinction coefficients (col. 14, lines 42-43). Thus, where the analyte is an enzyme substrate, the pad may be impregnated with the appropriate enzyme or enzymes to produce a product that is measured (col. 15, lines 10-13). The production of a detectable signal produced by enzymes teach the marker agent. The method teaches a measurement dye zone wherein the zone is coated or impregnated with an indicator material that reacts with the enzyme treated sample to give an indication of the presence or amount of analyte in the sample (col. 16, lines 23-27). Thus the indicator material that reacts with the enzyme treated sample material is the marker agent.

Doshi et al., teach one type of RBC agglutinating agent is lectins, including *Phaseolous vulgaris* (col. 7, lines 46-48). Other agglutinating agents include antibodies

that have a binding affinity for a determinant present on the surface of red blood cells that recognizes antigenic surface constituents (col. 7-8, lines 65-8). Doshi et al, teach a minimum amount of antibody must be used in the blood separation device (col. 8, lines 43-45). Doshi et al., state that one skilled in the art will readily determine the optimum amount of antibody to be used in the method (col. 8, lines 49-51). Thus Doshi et al., teach using an appropriate concentration of antibody. The use of detergents where a lipophilic analyte is in the blood is disclosed (col. 15, lines 27-28). The detergents are anionic or cationic detergents (col. 15, lines 33). Thus the art teaches using cationic and anionic detergents. Doshi et al., teach using various sticking agents or adhesives (col. 15, lines 38-41). These sticking agents would meet the permeabilization agents. However, Doshi et al., do not teach the method being performed in an enclosed and sterile device and comprising selectively lysing the cells and recovering microbes with second filter having a pore size of about 0.3 $\mu$ m to less than 1 $\mu$ m which retains contaminating microbes and allows passage of cellular debris.

Aunet et al., teach agglutination and separation of blood products including devices and techniques. Aunet et al., teach subjecting a sample of the blood product to an aggregation treatment of the blood cells (col. 2, lines 56-63). Aunet et al., teach substantially eliminating aggregates formed by passage of the sample over a first filter (col. 3, lines 9-11). Aunet et al., teach a device comprising an enclosed and sterile housing, entry and exit ports 9col. 5-6, lines 67-3). See also Figures 1-2.

Zierdt et al., teach selectively lysing the cells and recovering microbes with second filter having a pore size of about 0.3 $\mu$ m to less than 1 $\mu$ m which retains

contaminating microbes and allows passage of cellular debris (page 74 col. 2 and page 75, col.1). Zierdt et al., running the lysed blood samples through a filter sized at 0.45um which thereby has a pore size of about 0.3um to less than 1um and can retain contaminating microbes yet allow passage of cellular debris (page 75, col.1). Zierdt et al., teach the superiority of the lysis-filtration procedures (page 75, col. 2). Zierdt et al., teach increased sensitivity in the detection of bacteremia (page 77, col. 1). Zierdt et al., teach techniques where blood sample was treated with a lysing solution to release intracellular bacteria and then membrane filtered which had the advantage of separating bacterial pathogens from all antibacterial properties of the blood including antibodies, complement, phagocytes and antibiotics (page 74, col.1).

Therefore, it would have been prima facie obvious at the time of applicants' invention to modify the method of Doshi et al., to include an enclosed and sterile device of Aunet et al., and the lysing step and second filter that retains contaminating microbes and allows passage of cellular debris as taught by Zierdt et al., because Zierdt et al., teach that the lysis reaction increases the amount of bacteria retained by the filter and thereby removed from the blood; while Aunet et al, teach a safe device to allow blood analysis without contamination. No more than routine skill would have been necessary to include an enclosed device, a lysis reagent and step in the method of detection, since the art teaches that it is desirable to rid a blood sample of substantially all blood cells since it is difficult to conduct an analysis of the blood components without interference from external sources and red blood cells when testing for microbial contamination. Moreover, there would have been a reasonable expectation of success

in this modification since the art teaches that the lysis reagent and step does not harm the contaminants yet prepares the blood sample for microbial detection and analysis without time consuming and expensive techniques. Finally it would have been obvious to incorporate the enclosed device of Aunet et al., and the lysis and second filter of Zierdt et al., into the method of detection as taught by Doshi et al., because the lysing solution is known to release intracellular bacteria and filtration is advantageous because it separates out bacterial pathogens without allowing further contamination from external sources; thus yielding predictable results to one of ordinary skill in the art at the time of the invention.

***Claim Rejections - 35 USC § 103***

6. Claims 6 and 7 are rejected under 35 U.S.C. 103(a) as being unpatentable Doshi et al., (US Patent 5,766,552) and Zierdt et al., (J. of Clinical Microbio. 1982. Vol. 15(1):74-77) further in view of Cathey et al., (US Patent 5,798,215).

The claims are drawn to a method for detecting contaminating microbes comprising a marker agent that comprises a fluorescent marker or an agent coupled to a fluorochrome or an enzyme enabling degradation of substrate thereby made fluorescent wherein the fluorescence is produced using an excitation laser and detected.

The teachings of Doshi et al., and Zierdt et al., have been discussed above. However neither teaches a fluorescent marker or an agent coupled to a fluorochrome or an enzyme enabling degradation of substrate thereby made fluorescent wherein the

fluorescence is detected by an excitation laser wherein the method is performed in an enclosed and sterile device.

Cathey et al., teach analyte detection assays wherein the assay platform comprises a filter (col. 6, lines 19-21). The separation means for separating sample components may be positioned in the flow path of the assay platform (col.6, lines 54-56). For example, a filter may be positioned such that in when samples comprise red blood cells, the red blood cells are retained while serum flows through the filter (col. 6, lines 56-60). Depending upon the nature of the sample, the sample may be subjected to prior treatment, such as filtration or cell separation (col. 12, lines 15-19). For blood, one may wish to remove red blood cells to provide plasma or serum (col. 12, lines 20-21). Upon substrate addition, the substrate flows into the main flow path, where it is converted by an enzyme to a detectable product (col. 14, lines 34-36). Cathey et al., the method being performed in an enclosed and sterile housing comprised within the device (Figures 1,2 and 4). Fluorescent labels or enzymes are preferred because they convert substrates to non-diffusible dyes that are used in signal producing systems (col. 13, lines 60-64). These signal systems also provide for wider testing capabilities and are useful in microbial detection/diagnosis (col. 13, lines 64-66). Optical signals which may be detected and related to the presence and/or amount of analyte in the sample include emissions, e.g. from fluorescent labels or the fluorescence of a quenching member of a signal producing system (col. 14, lines 53-56). The optical signals are detected by a wide variety of means including devices that measure absorbance, transmissions, diffraction, resonance which includes lasers (col. 15, lines 13-34).

Therefore, it would have been prima facie obvious at the time of applicants' invention to modify the method of Doshi et al., and Zierdt et al., to include a marker agent that comprises a fluorescent marker or an enzyme enabling degradation of substrate thereby made fluorescent wherein the fluorescence is detected by an excitation laser as taught by Cathey et al. because Cathey et al., teach that fluorescent labels convert substrates to non-diffusible dyes are used in signal producing systems. No more than routine skill would have been necessary to include a fluorescence marker in the method of detection, since the art teaches that it is desirable to use fluorescence detection signals to detect analytes and other microbes. Moreover, there would have been a reasonable expectation of success in this modification since only routine skill would have been required to use fluorescent agents coupled with an enzyme substrate when Doshi et al., already teach microbial detection with enzymatic substrates.

***Claim Rejections - 35 USC § 103***

7. Claims 9 and 13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Doshi et al., (US Patent 5,766,552), Aunet et al., (US Patent 4,933,092) and Zierdt et al., (J. of Clinical Microbio. 1982. Vol. 15(1):74-77) further in view of Besson-Faure et al. (US Patent 6,168,925).

The claims are drawn to a method for detecting contaminating microbes comprising a specific antibody to a platelet antigen such as anti-GpIIb/IIIa.

Doshi et al., Aunet et al., and Zierdt et al., have been discussed above however neither teaches a specific antibody to a platelet antigen such as anti-GpIIb/IIIa.

Besson-Faure et al., teach the anti-GpIIb/IIIa antibody as a specific antibody to a platelet antigen that causes aggregation. Besson-Faure et al., teach the analysis of platelet GpIIb/IIIa receptors (col. 1, lines 5-8). Activated platelets have this receptor which binds with very high affinity and causes aggregation of the platelets with each other (col. 1, lines 25-30). The activation of the platelets allows the receptor to bind with high affinity, which causes aggregation (col. 1, lines 27-31). The molecules also remain in circulation for long periods of time (col. 1, lines 57-60). Besson-Faure et al., teach anti-GpIIb/IIIa antibodies are publicly available (col. 3, lines 1-10).

Therefore, it would have been prima facie obvious at the time of applicants' invention to modify the method of Doshi et al., Aunet et al., and Zierdt et al., to include the anti-GpIIb/IIIa antibody as a specific antibody to a platelet antigen as taught by Besson-Faure et al., because Besson-Faure et al., teach the a superior aggregation properties of anti-GpIIb/IIIa. No more than routine skill would have been necessary to include anti-GpIIb/IIIa in the method of detection, since the Doshi, Aunet et al., and Zierdt et al., teach that it is desirable to use antibody agglutinating agents that are quick, efficient at cluster formation, and fast acting and Besson-Faure et al., teach the anti-GpIIb/IIIa agglutinating agent which efficiently causes high affinity agglutination. Moreover, there would have been a reasonable expectation of success in this modification since only routine skill would have been required to use antibodies as agglutinating agents when the prior art provides motivation for antibody agglutinating agents wherein the motivation is that antibodies are reactive, well known for agglutinating properties and recognize glycoproteins; and Besson-Faure et al., provide

commercially available anti-GpIIb/IIIa agglutinating antibodies that cause high affinity agglutination.

***Conclusion***

8. No claims allowed.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ja-Na Hines whose telephone number is 571-272-0859. The examiner can normally be reached Monday thru Thursday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor Robert Mondesi, can be reached on 571-272-0956. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/JaNa Hines/

Examiner, Art Unit 1645

/Robert B Mondesi/

Supervisory Patent Examiner, Art Unit 1645